20. (Amended) The method according to claim 19, wherein the modification is a deletion of from 0.1 to 3 kb of the BamH1 restriction fragment of the long terminal repeat of the viral genome.

21. (Amended) The method according to claim 20 wherein the deletion is from 0.7 to 0.8 kb.

22. (Amended) The method according to claim 13 wherein the mutant herpes simplex virus is strain 1716.

REMARKS

Reconsideration is requested.

Claims 13-22 are pending.

Claim 13 has been amended to obviate the Section 112, first paragraph, rejection of claims 13-22. The Examiner's apparent suggestion that the claims were enabled for intratumoral injection is acknowledged, with appreciation, and the claims have been amended accordingly, without prejudice, to advance prosecution. Withdrawal of the Section 112, first paragraph, rejection of claims 13-22 is requested.

The Section 112, second paragraph, rejection of claims 13-22 is obviated by the above. The claims have been amended to include the Examiner's helpful suggestions. Withdrawal of the Section 112, second paragraph, rejection of claims 13-22 is requested.

The Section 102 rejection of claims 13-20 over Martuza (U.S. Patent No. 6,139,834) is traversed. Reconsideration and withdrawal of the rejection are requested in view of the following distinguishing comments.

The present application is based on PCT/GB97/00232 which was filed January 27, 1997, and UK Applications 9601507.8 and 9623365.5, filed January 25, 1996 and November 9, 1996, respectively. The cited Martuza patent is only citable prior art in so far as the disclosure of the parent applications disclose the presently claimed subject matter. Specifically, the applicants note the application which issued as the cited Martuza patent is a continuation-in-part of an application which issued as U.S. Patent No. 5,585,096 which is in turn is a continuation-in-part of an application which issued as U.S. Patent No. 5,728,379. The application which issued as U.S. Patent No. 5,585,096, was filed June 23, 1994 and the application which issued as U.S. Patent No. 5,728,379, was filed June 7, 1995. As the Examiner has stated that the effective filing date of the cited Martuza patent is June 23, 1994, the applicants assume the Examiner is relying on the disclosure of U.S. Patent No. 5,585,096.[1] The applicants respectfully submit that the cited Martuza patent fails to provide an enabling disclosure of the presently claimed method and accordingly, the Section 102 rejection should be withdrawn.

The presently claimed invention provides a method for treating a non-neuronal cancer in an animal which comprises the steps of injecting intratumorally an effective amount of mutant herpes simplex virus which has been modified in the γ34.5 gene such

[1] The applicants are uncertain in this regard why the Examiner has relied on U.S. Patent No. 6,139,834, as opposed to either U.S. Patent No. 5,728,379 and/or U.S. Patent No. 5,585,096. Clarification is requested in the event the rejection is maintained.

that the gene is non-functional and that the mutant virus infects, replicates and lyses non-neuronal tumor cells in the mammal. The applicants respectfully submit U.S. Patent No. 6,139,834, in so far as it can be relied upon as citable prior art, fails to teach each and every aspect of the presently claimed invention. Withdrawal of the Section 102 of claims 13-20 over U.S. Patent No. 6,139,834, is therefore requested.

The applicants respectfully submit that U.S. Patent No. 5,585,096 fails to provide an enabling disclosure of the presently claimed invention. The Examiner relies on column 11, lines 45-57 of U.S. Patent 6,139,834 at page 9 of the Office Action dated March 15, 2001 (Paper No. 12), however the noted disclosure refers to "nervous system tumors" while the presently claimed invention provides a method of treating a non-neuronal cancer. As for the suggestion in U.S. Patent No. 6,139,834, that other kinds of tumor cells may be killed (see, column 3, lines 61-67 and page 9 of Paper No. 12) the applicants respectfully submit that the patent only exemplifies the treatment of neuronal tumors and specifically gliomas. The cited patent fails to provide a detailed teaching of the treatment of non-neuronal tumors such that the applicants believe the cited patent fails to enable the presently claimed invention. Withdrawal of the Section 102 rejection of claims 13-20 over Martuza (U.S. Patent No. 6,139,834) is requested.

The Section 103 rejection of claims 13 and 19-22 over Martuza (U.S. Patent No. 6,139,834) in view of MacLean (Journal of General Virology 72:631-639, 1991) or Brown (WO 92/13943) and Markert (Neurosurgery 32:597-603, 1993) is traversed. Reconsideration and withdrawal of the rejection are requested in view of the following distinguishing remarks.

The secondary references fail to cure the deficiencies of Martuza cited above. The applicants respectfully submit that it was not known, and indeed the art taught away from, the use of mutant HSV according to the invention, for treating non-neuronal tumor cells. It was known at the filing date that HSV genomes could be altered in the γ34.5 genes such that they would become avirulent. It was also known that HSV inhabits neuronal cells and that mutated HSV has antineoplastic affects on glioma cells. The affect on glioma cells followed the line of thinking that the use of HSV was limited to neuronal cells. This is supported by Martuza U.S. Patent No. 5,585,096, which exemplifies the use of a mutant HSV on various neuronal tumor cells and glioma cells.

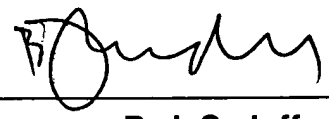
More specifically, the Martuza U.S. Patent No. 5,585,096 may be considered to provide guidance to one of ordinary skill in the art to try mutated HSV on non-neuronal tumor cells however given the negative teaching in the art and the unsubstantiated and speculative statements in the U.S. Patent No. 5,585,096, the applicants believe the ordinarily skilled person would not have thought it likely that non-neuronal cancer could be treated in the manner which is presently claimed.

Further, as with Martuza, the applicants respectfully submit that none of the cited art, considered alone or in combination, provide an enabling disclosure which would have placed the claimed invention in the possession of the public. Withdrawal of the Section 103 rejection of claims 13 and 19-22 is requested.

The claims are submitted to be in condition for allowance and a Notice to that effect is requested.

Respectfully submitted,

NIXON & VANDERHYE P.C.

By: 

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MARKED UP CLAIMS

13. (Amended) A method of treating a non-neuronal cancer in a mammal, [which] said method [comprises] comprising the [steps] step of[: administering to the mammal] injecting a mammal intratumorally with an effective amount of a mutant herpes simplex virus which has been modified in the γ34.5 gene such that the gene is non-functional[; and achieving infection and replication of the virus and lysis of a] , and wherein the mutant virus infects, replicates and lyses said non-neuronal tumor cell in the mammal [by the virus], thereby treating the non-neuronal cancer.

14. (Amended) [A] The method according to claim 13, where in the mammal is a human.

15. (Amended) [A] The method according to claim 13 or claim 14 wherein the cancer is a primary tumor.

16. (Amended) [A] The method according to claim 13 or claim 14 where the cancer is a metastatic tumor.

17. (Amended) [A] The method according to claim 13 or claim 14 wherein the cancer is a mesothelioma, ovarian carcinoma, bladder cancer or melanoma.

18. (Amended) [A] The method according to claim 13 wherein the mutant herpes simplex virus is a type 1 herpes simplex virus.

19. (Amended) [A] The method according to claim 13 wherein the mutant herpes simplex virus has been modified within the BamH1 restriction fragment of the long terminal repeat of the viral genome.

20. (Amended) [A] The method according to claim 19, wherein the modification is a deletion of from 0.1 to 3 kb of the BamH1 restriction fragment of the long terminal repeat of the viral genome.

21. (Amended) [A] The method according to claim 20 wherein the deletion is from 0.7 to 0.8 kb.

22. (Amended) [A] The method according to claim 13 wherein the mutant herpes simplex virus is strain 1716.